Please add the following new claims:

~~54~~ ~~52~~ --35. (New) A method as in claim 1, wherein said non-immune, noninflammatory condition is selected from the group consisting of: chronic diabetic nephropathy, diabetic glomerulopathy, diabetic renal hypertrophy, hypertensive nephrosclerosis, hypertensive glomerulosclerosis, renal dysplasia, glomerular hypertrophy, tubular hypertrophy, glomerulosclerosis and tubulointerstitial sclerosis.

~~36.~~ (New) A method as in claim 2, wherein said non-immune, noninflammatory condition is selected from the group consisting of: chronic diabetic nephropathy, diabetic glomerulopathy, diabetic renal hypertrophy, hypertensive nephrosclerosis, hypertensive glomerulosclerosis, renal dysplasia, glomerular hypertrophy, tubular hypertrophy, glomerulosclerosis and tubulointerstitial sclerosis.--

REMARKS

Upon entry of the foregoing amendments, claims 1-4, 6-10, 12, 15-17, 24, 28, 32–34 and new claims 35 and 36 are pending in the present application.

Applicants have amended claim 1 to recite "methods for improving renal function in a mammal in, or at risk of, chronic renal failure." Support for this amendment can be found at pg. 6, lines 1-3; pg. 8, line 23 through pg. 11, line 13. Applicants have amended claim 2 to recite the corresponding process step that relates back to the claim preamble. Support for this amendment can be found in claim 2 as originally filed. Applicants have also amended claims 1–4, 6–10, 12, 33 and 34 to more clearly define that the polypeptides of the present invention. Thus, claims 1–4, 6–10, 12, 33 and 34 have been amended to replace "OP/BMP renal therapeutic agent" with the term "morphogen." Support for this amendment can be found at pg. 1, lines 5-7 and pg. 13 line 1 through pg. 16, line 24. Applicants have also amended claims 1–4, 6–10, 12, 33 and 34 to more clearly define that the present methods are directed to mammals that are *not* kidney transplant recipients and are afflicted with non-immune, noninflammatory condition. Support for this amendment can be found at pg. 4, lines 19-26; and pg. 11, line 14 through pg. 12, line 14. New claims 35 and 36 are directed to specific non-immune, non-inflammatory conditions. Support for new claims 35 and 36 can be found in claim 1.

No new matter has been added by the present amendments.

THE 35 U.S.C. §112, FIRST PARAGRAPH REJECTIONS

The Examiner rejected claims 1–4, 6–10, 12, 15–17, 24, 28 and 32–34 under 35 U.S.C. §112, first paragraph, stating that "[t]he specification , while being enabling for the treatment of a mammal at risk of chronic renal failure, does not reasonably provide enablement for the treatment of a mammal in chronic renal failure." Specifically, the Examiner has alleged that the treatment of chronic renal failure and the improvement of renal function implies the "reversal of chronic renal failure."

The present invention is directed to methods of treatment for a mammal in or at risk of chronic renal failure. The invention as claimed **is not directed to the reversal of chronic renal failure**, and Applicants are not claiming methods for the reversal of chronic renal failure. **Applicants are claiming methods for *improving renal function* and methods to *delay the need for, or reduce the frequency of, chronic dialysis treatments.*** Although Applicants appreciate that the Examiner acknowledges that the present claims are enabled for mammals *at risk* of chronic renal failure, Applicants assert that the Specification is enabled for mammals *in* chronic renal failure. In short, the experimental models exhibited in Example 1 are directed to animals actually *in* chronic renal failure (by having a large portion of their kidneys removed). Specifically, the present application contains numerous examples directed to the ability of a morphogen to improve renal function, and consequently, reduce the need for or frequency of chronic dialysis treatments. The results of the disclosed Examples indicate that:

> OP-1 treated rats showed greater preservation or maintenance of glomeruli, as well as proximal and distal tubule structures,... and that **OP-1 treatment of nephrectomized rats resulted in the overall improvement (or reduced degeneration) of kidney tissue morphology, increased mesangial or perivascular thickening, decreased glomerular sclerosis and loop collapse, decreased presence of 'scattered' sclerosis and microaneurysms, and an increase in viable glomeruli.**

See e.g., Example 1, pg. 31 through pg. 33; and FIG. 6. , The Examiner has alleged

The Examiner has additionally rejected claims 1–4, 6–10, 12, 15–17, 24, 28 and 32 under 35 U.S.C. §112, first paragraph, stating that the Specification does not provide "enablement for a method of treatment comprising administering a protein having the recited %homology and % identity to OP-1 or the C-terminal seven cysteine domain thereof."

Specifically, the Examiner has maintained that:

> The assertions that these disparate proteins would have a similar activity can not be accepted in the absence of supporting evidence because the relevant literature teaches that individual members of the TGF-β superfamily, or a sub-group thereof, do not necessarily share the same biological activities. May 9, 2000 Office Action, pg. 4, lines 2–5.

The present invention teaches the administration of ***"bone morphogenic proteins,"*** not TGF-β. TGF-β is not a morphogen.

The Examiner has also stated that "[i]n general, the art recognizes that function can not be predicted on structural information alone."

Applicants agree. Accordingly, Applicants had previously amended the present claims to include the functional limitation wherein the claimed morphogens "induce chondrogenesis in an *in vivo* ectopic bone assay." Thus, according the claims, the present invention is the use of a morphogen which has 70% homology with the C-terminal seven-cysteine skeleton of OP-1 **and** can induce chondrogenesis in an *in vivo* ectopic bone assay.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph.

THE 35 U.S.C. §112, SECOND PARAGRAPH REJECTION

The Examiner has rejected claims 1–4, 6–10, 12, 15–17, 24, 28 and 32 under 35 U.S.C. §112, second paragraph, as being indefinite because the recite the term "OP/BMNP renal therapeutic agent" and because they fail to recite a process step which relates back to the claim preamble.

Applicants have amended claims 1–4, 6–10, 12, 33 and 34 to more clearly define that the polypeptides of the present invention. Thus, claims 1–4, 6–10, 12, 33 and 34 have been amended to replace "OP/BMP renal therapeutic agent" with the term "morphogen." Support for this amendment can be found at pg. 1, lines 5-7 and pg. 13 line 1 through pg. 16, line 24. Applicants believe that this amendment renders the rejection under 35 U.S.C. §112, second paragraph moot.

Applicants have also amended independent claims 1 and 2 to recite process steps that clearly relate back to the claim preamble. Specifically, the preamble of claim 1 now recites a method for "improving renal function in a mammal," while claim 2 recites the process step "such that said mammal's need for chronic dialysis is delayed or reduced." Basis for these amendments can be found in originally filed claims 1 and 2. Applicants believe that these amendments render the rejection under 35 U.S.C. §112, second paragraph moot.

The Examiner has also rejected claims 6–10 because there is insufficient basis for the limitation "said protein."

Applicants have amended claims 6 to now recite "said morphogen." Applicants believe that this amendment renders the rejection under 35 U.S.C. §112, second paragraph moot.

THE 35 U.S.C. §103(A) REJECTION

The Examiner has maintained the rejection of claims 1-4, 6-10, 12-17, 24, 28, and 32–34 under 35 U.S.C. §103(a) as being unpatentably obvious over Kubersampath (BB) in view of Tolins (u18), Ponticelli (v18), Klahr (w18), Watanabe (x18), Kees-Folts (y18), Glassock (v6), Brenner (u6), Coe (z18) and Glaasock (uu18).

Applicants disagree. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 985, 180 USPQ 580 (CCPA 1974); MPEP § 2143.03. "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson,* 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). Specifically, the Examiner stated at page 7 of the May 12, 1999 Office action:

> Kubersampath teaches the administration of a morphogen, OP1, to a kidney transplant...Kubersampath teaches that damage to cells resulting from the effects of inflammatory response by immune cells mediated tissue destruction has been implicated as the cause of reduced tissue function or loss of tissue function in the kidney...**Kubersampath is silent with respect to the treatment of patients afflicted with the recited conditions and the improvement of renal function therein.**

Further, all of the other cited references, (*i.e.* Tolin, Ponticelli, Klahr, Watanabe, Kees-Folts, Glassock, Brenner, and Coe) **do not teach, or even mention, the use of a morphogen to improve renal function and to delay the need for, or reduce the frequency of, chronic**

dialysis treatments in a mammal in, or at risk of, chronic renal failure. In fact, all of these subsequent references are directed to inflammatory and/or immune-associated renal conditions.

However, Applicants have amended the pending claims in order to expedite prosecution and allowance of the present application. As amended herein, the claims are limited to **mammals that are not kidney transplant recipients, and that are afflicted with non-immune, noninflammatory conditions**.

Accordingly, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

PROVISIONAL DOUBLE PATENTING REJECTIONS

Claims 1–4, 6–10, 12, 15–17, 24, 28 and 32–34 are provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over copending USSN 08/643,321.

Applicants will file a terminal disclaimer in compliance with 37 C.F.R. §1.321(c) upon the notification of allowable subject matter.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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